methods of using the novel folate receptor 1 antibodies or immunoconjugates to inhibit tumor growth and/or treat cancer.

[0013] Thus, in one aspect, the invention provides a humanized antibody or antigen binding fragment thereof that specifically binds a human folate receptor 1, wherein the antibody comprises (a) a heavy chain CDR1 comprising GYFMN (SEQ ID NO:1); a heavy chain CDR2 comprising RIHPYDGDTFYNQXaa$_1$FXaa$_2$Xaa$_3$ (SEQ ID NO:56); and a heavy chain CDR3 comprising YDGSRAMDY (SEQ ID NO:3); and (b) a light chain CDR1 comprising KASQSVSFAGTSLMH (SEQ ID NO:7); a light chain CDR2 comprising RASNLEA (SEQ ID NO:8); and a light chain CDR3 comprising QQSREYPYT (SEQ ID NO:9); wherein Xaa$_1$ is selected from K, Q, H, and R; Xaa$_2$ is selected from Q, H, N, and R; and Xaa$_3$ is selected from G, E, T, S, A, and V. In a certain embodiment, the humanized antibody or antigen binding fragment thereof binds a human folate receptor 1 with substantially the same affinity as the antibody chimeric Mov19. In a certain embodiment, the humanized antibody or antigen binding fragment thereof comprises the heavy chain CDR2 sequence RIHPYDGDTFYNQKFQG (SEQ ID NO:2).

[0014] In a certain embodiment, the binding affinity is measured by flow cytometry, Biacore, or radioimmunoassay.

[0015] In another embodiment, the invention provides a humanized antibody or antigen binding fragment thereof that specifically binds a human folate receptor 1, wherein the antibody comprises: (a) a heavy chain CDR1 comprising GYFMN (SEQ ID NO:1), or a variant thereof comprising 1, 2, 3, or 4 conservative amino acid substitutions; a heavy chain CDR2 comprising RIHPYDGDTFYNQKFQG (SEQ ID NO:2), or a variant thereof comprising 1, 2, 3, or 4 amino conservative acid substitutions; and a heavy chain CDR3 comprising YDGSRAMDY (SEQ ID NO:3), or a variant thereof comprising 1, 2, 3, or 4 conservative amino acid substitutions; and/or (b) a light chain CDR1 comprising KASQSVSFAGTSLMH (SEQ ID NO:7), or a variant thereof comprising 1, 2, 3, or 4 conservative amino acid substitutions; a light chain CDR2 comprising RASNLEA (SEQ ID NO:8), or a variant thereof comprising 1, 2, 3, or 4 conservative amino acid substitutions; and a light chain CDR3 comprising QQSREYPYT (SEQ ID NO:9), or a variant thereof comprising 1, 2, 3, or 4 conservative amino acid substitutions.

[0016] In a certain embodiment, the invention provides a humanized antibody or antigen binding fragment thereof that specifically binds the human folate receptor 1 comprising the heavy chain of SEQ ID NO:6. In another embodiment, the humanized antibody or antigen binding fragment thereof is encoded by the plasmid DNA deposited with the ATCC on Apr. 7, 2010 and having ATCC deposit nos. PTA-10772 and PTA-10773 or 10774.

[0017] In a certain embodiment, the invention provides a humanized antibody or antigen binding fragment thereof that competes for binding to FOLR1 with an antibody comprising (a) a heavy chain CDR1 comprising GYFMN (SEQ ID NO:1); a heavy chain CDR2 comprising RIHPYDGDTFYNQXaa$_1$FXaa$_2$Xaa$_3$ (SEQ ID NO:56); and a heavy chain CDR3 comprising YDGSRAMDY (SEQ ID NO:3); and (b) a light chain CDR1 comprising KASQSVSFAGTSLMH (SEQ ID NO:7); a light chain CDR2 comprising RASNLEA (SEQ ID NO:8); and a light chain CDR3 comprising QQSREYPYT (SEQ ID NO:9); wherein Xaa$_1$ is selected from K, Q, H, and R; Xaa$_2$ is selected from Q, H, N, and R; and Xaa$_3$ is selected from G, E, T, S, A, and V. In a certain embodiment, the humanized antibody comprises the heavy chain CDR2 sequence RIHPYDGDTFYNQKFQG (SEQ ID NO:2).

[0018] In a certain embodiment, the invention provides a polypeptide, humanized antibody or antigen binding fragment thereof comprising a heavy chain variable domain at least about 90% identical to SEQ ID NO:4, and a light chain variable domain at least about 90% identical to SEQ ID NO:10 or SEQ ID NO:11. In another embodiment, the humanized antibody or antigen binding fragment comprises a heavy chain variable domain at least about 95% identical to SEQ ID NO:4, and a light chain variable domain at least about 95% identical to SEQ ID NO:10 or SEQ ID NO:11. In a further embodiment, the humanized antibody comprises a heavy chain variable domain at least about 99% identical to SEQ ID NO:4, and a light chain variable domain at least about 99% identical to SEQ ID NO:10 or SEQ ID NO:11. In a certain embodiment, the humanized antibody comprises the heavy chain variable domain of SEQ ID NO:4, and the light chain variable domain of SEQ ID NO:10 or SEQ ID NO:11. In certain embodiments, the invention provides a polypeptide, antibody, or antigen binding fragment at least about 90% identical to SEQ ID NOs: 88-119. In certain embodiments, the invention provides a polypeptide, antibody, or antigen binding fragment at least about 95% identical to SEQ ID NOs: 88-119. In certain embodiments, the invention provides a polypeptide, antibody, or antigen binding fragment at least about 99% identical to SEQ ID NOs: 88-119.

[0019] In a certain embodiment, the invention provides a humanized antibody or antigen binding fragment thereof that is expressed at least ten-fold higher than chMov19 in eukaryotic cells. In a certain embodiment, the eukaryotic cells are HEK-293T cells.

[0020] In certain embodiments, the invention provides an antibody or antigen binding fragment thereof that specifically binds a human folate receptor 1, wherein the antibody comprises:

(a) a heavy chain CDR1 comprising SSYGMS (SEQ ID NO:30); a heavy chain CDR2 comprising TISSGGSYTY (SEQ ID NO:31); and/or a heavy chain CDR3 comprising DGEGGLYAMDY (SEQ ID NO:32); and/or (b) a light chain CDR1 comprising KASDHINNWLA (SEQ ID NO:27); a light chain CDR2 comprising GATSLET (SEQ ID NO:28); and a light chain CDR3 comprising QQYWSTPFT (SEQ ID NO:29). In another embodiment, the invention provides an antibody or antigen binding fragment thereof that specifically binds a human folate receptor 1, wherein the antibody comprises: (a) a heavy chain CDR1 comprising TNYWMQ (SEQ ID NO:60); a heavy chain CDR2 comprising AIYPGNGDSR (SEQ ID NO:61); and/or a heavy chain CDR3 comprising RDGNYAAY (SEQ ID NO:62); and/or (b) a light chain CDR1 comprising RASENIYSNLA (SEQ ID NO:57); a light chain CDR2 comprising AATNLAD (SEQ ID NO:58); and a light chain CDR3 comprising QHFWASPYT (SEQ ID NO:59). In another embodiment, the invention provides an antibody or antigen binding fragment thereof that specifically binds a human folate receptor 1, wherein the antibody comprises: (a) a heavy chain CDR1 comprising TNYWMY (SEQ ID NO:66); a heavy chain CDR2 comprising AIYPGNSDTT (SEQ ID NO:67); and/or a heavy chain CDR3 comprising